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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/424,059	11/18/1999	YOICHI NUNOKAWA	001560-376	7507

7590 09/24/2003

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EXAMINER
TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
1624	25

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/424,059	NUNOKAWA ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10, 17-25, and 38-41, and 44-73.* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *44-52* is/are allowed.

6)☒ Claim(s) *2-10, 17-25, and 38-41, and 53-73.* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

NON-FINAL ACTION

Applicant's amendment of 6-17-03 has been fully considered. Applicant's argument and amended claims have not overcome the previous rejections of 112/2nd, and 103. Thus, said rejections are maintained herein. New claims 44-73 raise the following new 112/2nd paragraph rejections. Claims 1, 11-16, 26-37, 42, and 43 are cancelled, leaving claims 2-10, 17-25, and 38-41 remaining for consideration along with new claims 44-73.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 2-10, 17-25, and 38-41 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claims 38 recites "A method for inhibiting NF-κB comprising administering to a patient in need of NF-κB inhibition....", which is unclear as to the diseases a patient has. The inhibition of NF-κB is at cellular level, thus, it is unclear as to the manifestation of NF-κB in a patient that would need such a claimed method.

b. Claim 40 recites "A method for inhibiting TNF-α production comprising administering to a patient in need of TNF-α inhibition....", which is unclear as to the diseases a patient has. The inhibition of TNF-α is at cellular level, thus, it is unclear as to the manifestation of TNF-α in a patient that would need such a claimed method.

c. Claims 39, and 41 are unclear because their metes and bounds are indefinite. They recite methods of preventing or treating a disease based on the mechanism of action (i.e., inhibiting NF-κB, and inhibiting TNF-α production). Said mechanism seems to treat a number of similar diseases. While overlapping treatments do not render a claim indefinite, they do not set a definite boundary on the claimed method. Another words, based on the overlapping treatments, if a reference taught the inhibition of TNF-α production, would it anticipate or render obvious the claimed method of inhibiting NF-κB? When the metes and bounds of a claim cannot be determined, it is indefinite.

d. Claim 10 still lacks antecedent basis because it recites the limitation of "suppresses gene expression...", which is not recited in claim 38.

e. Claim 25 still lacks antecedent basis because it recites the limitation of "suppresses gene expression...", which is not recited in claim 40.

f. Claim 53 still lacks antecedent basis because it recites the limitation of "suppresses gene expression...", which is not recited in claim 44.

g. Claim 63 still lacks antecedent basis because it recites the limitation of "suppresses gene expression...", which is not recited in claim 54.

h. Claim 73 still lacks antecedent basis because it recites the limitation of "suppresses gene expression...", which is not recited in claim 64.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Scope of Enablment:** Claims 2-10, 17-25, 38-41, and 54-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of inflammatory diseases, does not reasonably provide enablement for other diseases such as autoimmune diseases, and viral infections that are allegedly related to the inhibition of NF-κB, and production of TNF-α. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The quantity of experimentation necessary;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The breadth of the claims;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The Quantity of Experimentation Necessary: Autoimmune diseases encompasses many diseases of different organs, and tissues. For example, psoriasis and lupus are also considered as autoiummune diseases, and so is HIV. Likewise, viral infection includes "common cold", cold sore, shingles, chicken pox, influenza, etc. All such diseases do not affect the same target tissue, or organ, nor do they share the same etiology. While the literature relates NF-κB, and TNF-α with many diseases' pathophysiology, there is no correlation that a particular set of compounds (e.g., benzoquinone) can treat all kind of diseases that are allegedly related to NF-κB, or TNF-α.

The Amount of Guidance Presented: The specification only shows that the claimed benzoquinone compounds can inhibit NF-κB, and the production of TNF-α. It does not shows if said compounds can actually treat any autoimmune diseases, nor does it show that said compounds can inhibit viral replication. Thus, there is insufficient guidance for one skilled in the art to treat autoimmune diseases, and viral infection using the claimed benzoquinone.

The State of the Prior Art: As evidence by the teaching of Suntory (discussed below), the benzoquinone compounds is only effective in the treatment of post cerebral embolism

symptom, as well as related complications. There is no suggestion that said compounds are effective in treating other diseases.

The Relative Skill of Those in the Art: Even with the highly skilled clinician, it would take more than routine experimentation to treat autoimmune diseases and viral infections using the claimed compounds.

The Predictability or Unpredictability of the Art: The pharmaceutical art has always been unpredictable especially when there is no correlation between a set of compounds and the type of disease. In the instant case, no correlation has been established between the claimed benzoquinone with the treatment of autoimmune diseases, viral infections, or other diseases that are related to NF-κB, or TNF-α.

The Breadth of the Claims: Claims 38 and 40 recites "a method for inhibiting...", which reads on the treatment of many unknown diseases. Claims 39 and 41 even recite the prevention of many diseases which the specification does not have evidence for. Claim 54 recites "a method for treatment of autoimmune diseases..." which covers many diseases that may not even be related to NF-κB or TNF-α. Claim 64 recites "a method for treatment of viral diseases..." which encompasses many diseases that are caused by various viri, and are not known to be treated by the same agent. With claims of such a broad scope of inhibiting, prevention, treatment, etc., one skilled in the art would have to carry out undue experimentation to treat all diseases related to NF-κB, and TNF-α using the claimed benzoquinone compounds.

Claim Rejections - 35 USC § 103

The examiner is withdrawing the previous 103 rejection, and rewriting it to clarify the specific teachings and their relationships since applicant's arguments seem to need clarification of these references.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-9, 17-24, and 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Suntory Ltd.** (JP 62-286949) in view of **Vassalli** and **Baeuerle**. It is true that Suntory alone does not motivate one skilled in the art to use the claimed benzoquinone for inhibiting NF-κB, or inhibiting TNF-α production. However, the **combination of all three teachings would have motivated one skilled in the art to** extend the application of the claimed benzoquinone compounds to the inhibition of NF-κB, or inhibition of TNF-α production.

First, the teaching of **Suntory** allows one skilled in the art to use the benzoquinone compounds in the treatment of post cerebral embolism symptom, post cerebral hemorrhage symptom, etc. Said symptoms are related to **blood clot**. Suntory's teaching differs from the instant invention in that there is no specific mention of TNF or NF-κB.

However, in a generic teaching, **Vassalli** correlates the action of TNF with clotting promoting activity (see page 419, the paragraph titled *"Effects on the coagulation system"*). Thus, it directs one to note that inhibiting TNF's action or production would treat blood clot, and in turn treat embolism. Of course, the less TNF available, the less chance for blood to clot.

Also a second generic teaching by **Baeuerle et. al.** relates the action of NF-κB to a number of conditions including thrombin which can cause embolism(see Table II). Again, it directs one to note that inhibiting NF-κB would treat embolism as well.

Thus, from all three teachings, one could conclude that if a compound could treat an embolism such as cerebral embolism, then its underlying mechanism would be the inhibition of TNF's production or inhibition of NF-κB's activity.

Therefore, at the time of the invention, it would have been obvious to one skilled in the art to use the benzoquinone compounds of **Suntory** in the method of inhibiting NF-κB, or inhibiting the production of TNF-α as taught by **Vassalli** and **Baeuerle et. al.**

Allowable Subject Matter

5. Claims 44-52 are allowed because the teaching of Suntory does not suggest the benzoquinone compounds can treat inflammatory. The teachings of Vassalli and Baeuerle et. al. do not provide nexus for bridging gap between the teaching of Suntory and the claimed methods of treatment.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (5:00-12:30) & every Saturday morning (starting from 4-7-03).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong
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September 22, 2003

Art Unit 1621
JEAN F. VOLLANO
PRIMARY EXAMINER